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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/529,008	01/03/2006	Sanjay Suri	05-40052-US	8800

7590
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2500 One Liberty Place
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EXAMINER

DESAI, RITA J

ART UNIT	PAPER NUMBER
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1625

MAIL DATE	DELIVERY MODE
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03/05/2009

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/529,008	Applicant(s) SURI ET AL.	
	Examiner Rita J. Desai	Art Unit 1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 05 December 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-20 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-20 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

Art Unit: 1625

DETAILED ACTION

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 12/5/08 has been entered.

Claims 1-20 are pending.

Response to applicants arguments.

Applicants argue regarding the WO '95 document that the reaction is faster in the aq solvent according to Peon But that is incorrect as the abstract teaches that **In methanol, proton transfer occurs with a time constant of 9.0 ps, making this the fastest known intermolecular proton- transfer reaction to carbon.** Also in the presence of an inorganic base which is also made in water. Thus there is some water present.

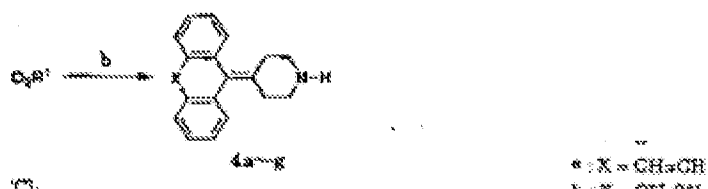
Regarding the Iwasaki reference applicants argue the examiner has not given proper rational and the compounds are not drawn to desloratadine.

See page 2289 preparation of compound 4a.

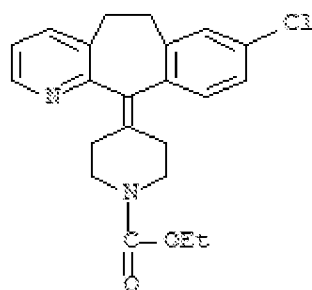
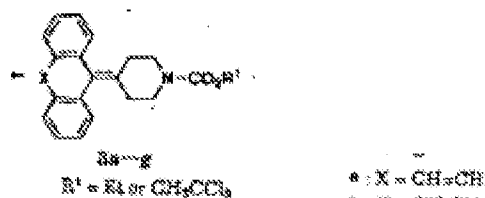
4-(5,5'-Dibenz[*a,h*]cyclohept-3-ylidene)piperidine (4a). A mixture of 3a (63.6 g, 0.19 mol) and KOH (32.0 g, 0.37 mol) in *n*-BuOH (250 ml) was refluxed for 2 h. After removal of the solvent under reduced pressure, the residue was diluted with water and extracted with toluene. The organic layer was washed with water, dried over Na_2SO_4 , and evaporated to afford 4a as pale yellow crystals (47.9 g, 92%). The free base was converted to the hydrochloride by the usual method.

Compound 4a has the formula as given below:-

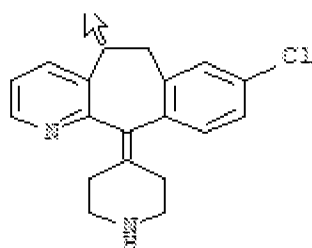
Art Unit: 1625



Compound 3a which is the starting material has the formula :



Loratadine is



Desloratadine is

According to KSR v Teleflex 2005, The motivation comes from the fact that is obvious to try with a reasonable expectation of success. The rational according to KSR is given by obvious to try with an expectation of success.

Art Unit: 1625

(E) "Obvious to try"—choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

Similar reaction is clearly

taught in the WO'95 reference. As given above, the same reagents are also taught water, base and alcohols. All the claim limitations are there in the prior art. The improvement is not clearly defined in the claims and changing the order or making slight modifications in the concentration is within the scope of routine experimentation.

The compounds in Iwasaki are very similar. The difference is only of the substituted chlorine which position is passive in the reaction.

The process clearly teaches adding a base in the presence of alcohol.

US 5595997 discloses the same with respect to Loratadine to make its metabolite, which would be desloratadine.

Loratadine (4.0 g) was added to a solution of sodium hydroxide (5.9 g) in 280 mL of absolute ethanol and the mixture was stirred at reflux for four days. The mixture was cooled and concentrated to remove ethanol. The residue was diluted with water and aqueous layer was extracted with methylene chloride five times. The combined organic layer was washed with water, brine and dried over sodium sulfate. The solvent was evaporated to give 2.82 g (87%) of pure loratadine derivative (or metabolite) as a pale-tan solid.

There are other solvents and reagents given but again applicants claim is drawn to a process "comprising" thus other steps can be included.

The arguments based on Peon disclosure is not convincing. The reaction would have some water whether it was neat alcohol or a diluted alcohol.

Art Unit: 1625

The arguments over Sejas reference is also not convincing.

The Peon reference teaches

All the above rejections also in view of Peon Jorge et al , 2001 Solvent reorganization Controls the rate of proton transfer ...

Jorge et al , 2001 teaches that the proton transfer in neat solvents especially in methanol is fastest . See abstract.

from an alcohol molecule to singlet diphenylcarbene. Since a shell of solvent molecules surrounds each nascent carbene, **the intrinsic rate of protonation in the absence of diffusion could be measured. In methanol, proton transfer occurs with a time constant of 9.0 ps, making this the fastest known intermolecular proton- transfer reaction to carbon.**

In O-deuterated methanol proton transfer occurs in 15.0 ps. Slower rates were observed in the longer alcohols. The protonation times correlate reasonably well with solvation times in these alcohols, suggesting that solvent fluctuations are the rate-limiting step. In all alcohols studied, the carbocations decay on a somewhat slower time scale to yield diphenylalkyl ethers. In methanol and ethanol the rate of decay is determined by reaction with neutral solvent nucleophiles. There is evidence in 2-propanol that geminate, reaction within the initial ion pair is faster than reaction with solvent. No isotope effect was

Arguments with respect to WO'96 document is also not convincing. Peon clearly teaches that reaction is very efficient in alcohol.

Even without this teaching the reference teaches using a base for the hydrolysis.

Again for the EP '855 reference applicants are arguing using the Peon teaching which is unclear to the examiner as in the abstract it teaches the efficiency of the methanol. See above.

The EP '897 the reasoning is the same as is the '716 patent , Hu '864 document.

It appears the applicant s are further arguing the above reference in view of Peon et al using the same reasoning as given in the above rejection.

The examiner does not find it convincing for the same reasons given above.

Art Unit: 1625

The examiner has made a prima-facie case with KSR v Teleflex 2005, obvious to try with an predictable expectation of success, rational.

According to KSR v Teleflex 2005, The motivation comes from the fact that is obvious to try with a reasonable expectation of success. The rational according to KSR is given by obvious to try with an expectation of success.

(E) "Obvious to try"—choosing from a finite number of identified, predictable solutions, with a reasonable expectation of success;

Similar reaction is clearly

taught in the WO'95 reference. As given above, the same reagents are also taught water, base and alcohols. All the claim limitations are there in the prior art. The improvement is not clearly defined in the claims and changing the order or making slight modifications in the concentration is within the scope of routine experimentation.

The previous rejections are maintained.

US 4659716 in column 4, lines 38-39 teaches using a neat t-butyl alcohol, in the process of preparing Loratadine.

about 50° C. to about 100° C. with t-butyl alcohol. The reaction may be performed with inert solvents but is usually run neat.

US 5595997 as disclosed in the specifications also uses absolute ethanol, which is same as neat

alcohol.

Loratadine (4.0 g) was added to a solution of sodium hydroxide (5.9 g) in 280 ml. of absolute ethanol and the mixture was stirred at reflux for four days. The mixture was cooled and concentrated to remove ethanol. The residue was diluted with water and aqueous layer was extracted with 10 methylene chloride five times. The combined organic layer was washed with water, brine and dried over sodium sulfate. The solvent was evaporated to give 2.62 g (87%) of pure loratadine derivative (or metabolite) as a pale-tan solid.

Art Unit: 1625

Applicants argue that the process teaches removing ethanol and then extraction with methylene chloride.

Applicants are reminded that their claims say comprises and would include routine steps.

Applicants claims are not limited to a certain amount of reflux time nor to not using any other solvent.

The motivation to use neat solvents comes from the prior art such as US 5595997 and US 4659716 . The US '997 patent uses it to make the Desloratadine and '716 uses it to make Loratadine.

It has been used before for the same and similar process motivating a person of skill to use it in the process.

New Rejection

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-20 are rejected under 35 U.S.C. 112, second paragraph, as failing to set forth the subject matter which applicant(s) regard as their invention.

A Jepson claim "improvement" claim has to have the phrase " wherein the improvement comprises," See M.P.E.P. 1.75(e) (2) .

Art Unit: 1625

M.P.E.P. § 1.75 Claim(s). - Appendix R Patent Rules

(e) Where the nature of the case admits, as in the case of an improvement, any independent claim should contain in the following order:

(1) A preamble comprising a general description of all the elements or steps of the claimed combination which are conventional or known,

(2) A phrase such as "wherein the improvement comprises," and

(3) Those elements, steps, and/or relationships which constitute that portion of the claimed combination which the applicant considers as the new or improved portion.

The previous rejections are maintained.

The rejection under 35 USC 103 as being unpatentable over WO -A-95 10514 ("WO 95"), Iwasaki et al., 1999, Chemical And Pharmaceutical Bulletin, JP (11-1999), Vol.42, pages 2285-2290 ("Iwasaki") Sejas et al., 1998, Tetrahedron, 44:6197-6200 ("Sejas") WO-A-9631478 ("WO 96"), EP 0,208,855 ("EP '855"), EP 0,152,897 ("EP '897"), US 4,659,716 ("716 patent"), or HU 194,864 ("HU '864") and US 5595997 all still stand.

US 4659716 in column 4, lines 38-39 teaches using a neat t-butyl alcohol, in the process of preparing Loratadine.

about 50° C. to about 100° C. with t-butyl alcohol. The reaction may be performed with inert solvents but is usually run neat.

US 5595997 as disclosed in the specifications also uses absolute ethanol, which is same as neat

alcohol.

Loratadine (4.0 g) was added to a solution of sodium hydroxide (5.9 g) in 250 ml. of absolute ethanol and the mixture was stirred in reflux for four days. The mixture was cooled and concentrated to remove ethanol. The residue was diluted with water and aqueous layer was extracted with 10 methylene chloride five times. The combined organic layer was washed with water, brine and dried over sodium sulfate. The solvent was evaporated to give 2.82 g (87%) of pure loratadine derivative (or metabolite) as a pale-tan solid.

Art Unit: 1625

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It has been used before for the same and similar process motivating a person of skill to use it

Conclusion

Claims 1-20 stand rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Rita J. Desai whose telephone number is 571-272-0684. The examiner can normally be reached on Monday - Friday, flex time..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Janet Andres can be reached on 571-272-0867. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1625

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Rita J. Desai/
Primary Examiner, Art Unit 1625

February 24, 2009